FORM PTO-1390 (REV 10-94) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

DOCKET #: 4271-30PUS

				U.S. APPLICATION NO. (If known, see 37 CFR 1.5)
				09/806558

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP99/07045	22 September 1999	30 September 1998

TITLE OF INVENTION

Pharmaceutically Active Plant Preparation for the Treatment of Migraine

APPLICANT(S) FOR DO/EO/US

Stefan SPIESS

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [x]This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371
3. [x]This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. [x]A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. [x]A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [x]is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [] has been transmitted by the International Bureau.
   c. [] is not required, as the application was filed in the United States Receiving Office (RO/US)
6. [x]A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. [x]Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [] have been transmitted by the International Bureau.
   c. [] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [x]have not been made and will not be made.
8. [] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. [x]An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [] A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. Below concern other document(s) or information included:

11. [] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [x]An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [x]A **FIRST** preliminary amendment.
    [] A **SECOND** or **SUBSEQUENT** preliminary amendment.
14. [] A substitute specification.
15. [] A change of power of attorney and/or address letter.

[x]Other items or information *(specify):* PCT Publication and Int'l Search Report

U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/806558	PCT/EP99/07045	4271-30PUS

17.[x]The following fees are submitted:

Basic National Fee (37 CFR 1.492(a)(1)-(5)):		
Search Report has been prepared by the EPO or JPO **$860.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.482)..... **$690.00**		
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) **$710.00**		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$1000.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4) **$100.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	**$**	860
Surcharge of **$130.00** for furnishing the oath or declaration later than [] 20 [] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	**$**	

Claims	Number Filed	Number Extra	Rate		
Total Claims	19 - 20 =		x **$18.00**	**$**	
Independent Claims	2 - 3 =		x **$80.00**	**$**	
Multiple dependent claim(s) (if applicable)			+ **$270.00**	**$**	
TOTAL OF ABOVE CALCULATIONS =				**$**	860
Reduction of ½ for filing by small entity, if applicable.				**$**	
SUBTOTAL =				**$**	860
Processing fee of **$130.00** for furnishing the English translation later than [] 20 [] 30 months from the earliest claimed priority date (37 CFR 1.492(f)). +				**$**	
TOTAL NATIONAL FEE =				**$**	860
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by the appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +				**$**	40
TOTAL FEES ENCLOSED					$900
Amount to be refunded:					**$**
charged:					**$**

a. [x]Two check(s) in the amount(s) of $ 860 and $ 40 to cover the above fees is/are enclosed.
b. [] Please charge my Deposit Account No. 03-2412 in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.
c. [x]The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 03-2412. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:
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Attorney Docket # 4271-30PUS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re National Phase PCT Application of

Stefan SPIESS

International Appln. No.: PCT/EP99/07045

International Filing Date: 22 September 1999

For: Pharmaceutically Active Plant Preparation for the Treatment of Migraine

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231
BOX PCT

S I R:

Prior to examination of the above-identified application please amend the application as follows:

In the Specification:

Referring to the English language translation:

Page 3, between the title and the first line of text insert as a centered heading --**Background of the Invention**--;

line 7 from the bottom, following "symptoms" and "vomiting" in each instance insert --, --;

Page 5, above the first line of text insert as a centered heading --**The Invention**--;

Page 8, following the last line of text insert as a separate paragraph --The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention in the use of such terms and expressions of excluding any equivalent of the features shown and described or portions thereof, it being recognized that various modifications are possible within the scope of the invention.--

In the Claims:

Without prejudice cancel claims 1 to 14 and add claims 15 to 33 as follows:

15. An herbal pharmaceutical preparation for the treatment of migraine, comprising: *Tanacetum parthenium* with at least one other plant component selected from the group consisting of *Vitex agnus-castus*, *Cimicifuga racemosa*, *Zingiber officinale* and combinations thereof.

16. The herbal pharmaceutical preparation for the treatment of migraine of claim 15, wherein components and/or preparations of the pharmaceutically active ingredients are used.

17. The herbal pharmaceutical preparation for the treatment of migraine of claim 15, wherein the preparation is in the form of an extract, powder, distillate, infusion, tincture, or oil.

18. The herbal pharmaceutical preparation for the treatment of migraine of claims 15, wherein the least one other plant component is *Vitex agnus-castus*.

19. The herbal pharmaceutical preparation for the treatment of migraine of claim 15, wherein the least one other plant component is *Cimicifuga racemosa*.

20. The herbal pharmaceutical preparation for the treatment of migraine of claim 15, wherein the least one other plant component is *Vitex agnus-castus* and *Zingiber officinale*.

21. The herbal pharmaceutical preparation for the treatment of migraine of claim 15, wherein the least one other plant component is *Zingiber officinale*.

22. The herbal pharmaceutical preparation for the treatment of migraine of claim 15, wherein the preparation is in the form of a capsule, a film coated tablet, a solution, a sugar-coated tablet, a suppository, an effervescent tablet, a chewable tablet, or an effervescent granulate for administration.

23. The herbal pharmaceutical preparation for the treatment of migraine of claim 15, wherein *Tanacetum parthenium* in the form of the plant component and/or a preparation is present in an amount of 0.1-1 mg, and preferably 0.2-0.6 mg of parthenolide.

24. The herbal pharmaceutical preparation for the treatment of migraine of claim 15, wherein *Cimicifuga racemosa* in the form of the plant component and/or a preparation is present is an amount of 20-100 mg.

25. The herbal pharmaceutical preparation for the treatment of migraine of claim 15, wherein *Vitex agnus-castus* in the form of the plant component and/or a preparation is present in an amount of 20-100 mg, preferrably 20-40 mg.

26. The herbal pharmaceutical preparation for the treatment of migraine of claim 15, wherein *Zingiber officinale* in the form of the plant component and/or a preparation is present is an amount of 0.5-6 g, and preferrably 1-4 g.

27. A method for the treatment or prevention of migraine in a subject in need of such treatment or prevention, comprising: administering to such a subject an effective amount of herbal components and/or a preparation of *Tanacetum parthenium* in combination with at least one other plant component selected from the group consisting of *Vitex agnus-castus, Cimicifuga racemosa, Zingiber officinale* and combinations thereof.

28. The method of claim 27 wherein said subject is a woman and the migraine is in association with her period, or of menstrual complaints or of additional gastrointestinal complaints.

29. The method of claim 27 wherein the preparation as selected from the group consisting of *Tanacetum parthenium* combined with *Vitex agnus-castus, Tanacetum parthenium* combined with *Cimicifuga racemosa, Tanacetum parthenium* combined with *Zingiber officinale*, and *Tanacetum parthenium* combined with *Vitex agnus-castus* and *Zingiber officinale.*

30. The method of claim 27 wherein *Tanacetum parthenium* is present in an amount of 0.1-1 mg, preferably 0.2-0.6 mg of parthenolide.

31. The method of claim 27 wherein *Cimicifuga racemosa* is present in an amount of 20-100 mg.

32. The method of claim 27 wherein *Vitex agnus-castus* is present in an amount of 20-100 mg, preferably 20-40 mg.

33. The method of claim 27 wherein *Zingiber officinale* is present in an amount of 0.5-6 g, preferably 1-4 g.

34. The method of claim 27 wherein the herbal components or preparation are administered in the form of a capsule, a film coated tablet, a solution, a sugar-coated tablet, a suppository, an effervescent tablet, a chewable tablet, or an effervescent granulate.--

In the Abstract:

Following page 11, insert as a new page the following abstract:

--**Abstract**

The invention relates to pharmaceutical combination preparations with synergistic action for the treatment of migraine. Said preparations contain plant-based components and/or preparations of Tanacerum parthenium in combination with Vitex agnus castus and/or Cimicifuga racemosa and/or Zingiber officinale as their pharmaceutically active ingredients. The combination preparation provided for in the invention is suitable for the treatment of not only the headache but also the other symptoms of migraine while avoiding the usual side-effects.--

REMARKS

The specification and claims of the above identified application have been amended to a form more consistent with U.S. practice.

Early consideration and allowance of the application with claims 15 to 34 are earnestly solicited.

Any fees or charges required at this time in connection with the application may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,
COHEN, PONTANI, LIEBERMAN & PAVANE

By: _____

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30 March 2001

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

Refer to the English language translation, page 3 between the title and the first line of text insert as a heading as follows:

--**Background of the Invention**--;

Line 7 from the bottom, following "symptoms" and "vomiting" in each instance insert --, --;

Migraine is understood today as a complex functional disturbance of neuronal and vascular elements of the CNS. The headaches associated with it are apparently induced by an aseptic inflammation of the blood vessels and the dura mater vessels of the brain in association with permeability of the vessel walls for albumin and the release of neurotransmitters such as serotonin and tryptamine. The disorder is characterized by the following sequence of events: vasodilation, activation of the trigeminus, and neurogenic inflammation. Migraine attacks occur abruptly and repeatedly. They involve headaches on one side of the head, which can be associated with various accompanying phenomena: autonomic symptoms such as nausea and vomiting, aversion to light and noise, visual symptoms such as disturbed vision, and also neurological breakdowns such as paralysis or disturbances in language or speech. The symptoms, nausea and vomiting, are caused by the absence of gastrointestinal peristalsis. Most (70%) migraine patients are women. They are more likely to suffer migraine during their menstrual periods. The treatment of migraine has been limited so far to the treatment of the headaches as a way of relieving the patient's discomfort. A more effective and improved

treatment of migraine by means of phytopharmaceutical preparations to address the other symptoms of migraine is not known.

Page 5, above the first line of text insert as a heading as follows:

--**The Invention**--;

Page 8, following the last line of text insert as a separate paragraph the following:

--The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention in the use of such terms and expressions of excluding any equivalent of the features shown and described or portions thereof, it being recognized that various modifications are possible within the scope of the invention.--

In the Abstract:

Following page 11, insert as a new page the following abstract:

--**Abstract**

The invention relates to pharmaceutical combination preparations with synergistic action for the treatment of migraine. Said preparations contain plant-based components and/or preparations of Tanacerum parthenium in combination with Vitex agnus castus and/or Cimicifuga racemosa and/or Zingiber officinale as their pharmaceutically active ingredients. The combination preparation provided for in the invention is suitable for the treatment of not only the headache but also the other symptoms of migraine while avoiding the usual side-effects.--

PHARMACEUTICALLY ACTIVE HERBAL PREPARATION FOR THE TREATMENT OF MIGRAINE

The invention pertains to a pharmaceutically active herbal preparation with improved effectiveness for the all-encompassing treatment of migraine, the preparation containing plant components and/or preparations of *Tanacetum parthenium* in combination with *Vitex agnus-castus* and/or *Cimicifuga racemosa* and/or *Zingiber officinale* as pharmaceutically active components.

Migraine is understood today as a complex functional disturbance of neuronal and vascular elements of the CNS. The headaches associated with it are apparently induced by an aseptic inflammation of the blood vessels and the dura mater vessels of the brain in association with permeability of the vessel walls for albumin and the release of neurotransmitters such as serotonin and tryptamine. The disorder is characterized by the following sequence of events: vasodilation, activation of the trigeminus, and neurogenic inflammation. Migraine attacks occur abruptly and repeatedly. They involve headaches on one side of the head, which can be associated with various accompanying phenomena: autonomic symptoms such as nausea and vomiting, aversion to light and noise, visual symptoms such as disturbed vision, and also neurological breakdowns such as paralysis or disturbances in language or speech. The symptoms nausea and vomiting are caused by the absence of gastrointestinal peristalsis. Most (70%) migraine patients are women. They are more likely to suffer migraine during their menstrual periods. The treatment of migraine has been limited so far to the treatment of the headaches as a way of relieving the patient's discomfort. A more effective and improved treatment of migraine by means of phytopharmaceutical preparations to address the other symptoms of migraine is not known.

Tanacetum parthenium (feverfew), which belongs to the Asteraceae family, is a traditional herbal remedy used to treat migraine. The flowering plant and especially the leaves of the English variety of *Tanacetum parthenium* contain ethereal oil, camphor, borneol, pinene, and above all sesquiterpene lactones. Sesquiterpene lactones which have been isolated include michefuscalide, *cis*-chrysanthenyl [*sic; chrysanthemyl? -- Tr. Ed.*] acetate, and parthenolide, which is the dominant component quantitatively and which therefore can be considered the chief substance. To treat migraine in any meaningful way with a drug, it must be possible to affect the parameters vascular disturbance, pain, and inflammation. The sesquiterpene lactones, especially parthenolide, have an antiphlogistic effect by inhibiting prostaglandin synthesis, improve the flow behavior of the blood by inhibiting platelet aggregation, reduce the release of serotonin, inhibit the release of histamine, and exert a spasmolytic effect. *Tanacetum parthenium* is administered in most cases for the sake of prevention. The psychological and physical symptoms typical of migraine are ameliorated by taking *Tanacetum parthenium*, but they often continue to be a considerable burden on the affected persons, with the result that the quality of life is severely impaired.

The active ingredients not of plant origin used to treat migraine such as sumatriptan, ibuprofen, acetylsalicylic acid, etc., also suffer from the problem that the success of the treatment is often insufficient, and there is also the danger of considerable side effects.

The task of the present invention is to provide a more effective phytopharmaceutical drug with improved efficacy for the treatment of migraine and with few if any side effects.

The surprising discovery has now been made that the task according to the invention can be accomplished by a combination of *Tanacetum parthenium* with other medicinal plants such as *Vitex agnus-castus* and/or *Cimicifuga racemosa* and/or *Zingiber officinale* (ginger). The combination of *Tanacetum parthenium* with *Zingiber officinale* leads to a significant improvement in efficacy; in addition to the alleviation of the headache, the other symptoms of migraine, including especially vertigo, nausea, and gastrointestinal complaints can also be minimized. The combination of *Tanacetum parthenium* with *Vitex agnus-castus* or *Cimicifuga racemosa* as well as the three-fold combination of *Tanacetum parthenium*, *Zingiber officinale*, and *Vitex agnus-castus* lead to a considerable enhancement of the effect or alleviation of all the symptoms of migraine, especially in women whose migraine attacks are concentrated in the time around their periods.

Vitex agnus-castus (monk's pepper, chaste tree) belongs to the Verbenaceae family (vervain, verbena). The fruits are the part of the plant which is used. Various secondary plant compounds have been detected as constituents such as iridoids, flavonoids, and ethereal oils. The ability of these compounds to direct their attack against lactotropic cells and to bind themselves to the dopamine receptors there explains why they are so effective in relieving premenstrual syndrome. The term "premenstrual syndrome" is understood to mean a recurring set of psychological and physical disturbances and/or changes in behavior, which normally can occur only in the corpus luteum phase of the menstrual cycle. The increase in prolactin secretion associated with this disorder is significantly reduced by the phytopharmaceutical of the invention. An excessive level of prolactin in the blood lowers pulsatile [*? -- Tr. Ed.*] gonadotropin secretion, which is ultimately the key factor in determining

a normal menstrual cycle.

Cimicifuga racemosa (snake root, bugbane) belongs to the Ranunculaceae family. The root is the part used for pharmaceutical purposes. The valuable constituents are the triterpene glycosides, especially the xylosides actein and cimicifugoside. The preparation made from the plant material has hormone-like properties, the estrogenic activity component being especially dominant. These herbal preparations are usually used to treat premenstrual syndrome and climacteric symptoms.

Zingiber officinale (ginger) is important throughout the world as a spice and as basic material in the food industry, but has also been used medicinally for centuries. It is the root of the *Zingiber officinale* plant which is used pharmaceutically; it contains up to 3% of ethereal oil (ginger oil), the chief components of which quantitatively are sesquiterpene hydrocarbons and sesquiterpene alcohols, primarily zingiberene (30%) and β-bisabolene (10-15%). In addition, it also contains various acrid compounds such as gingerols and shogaols, which are highly effective therapeutically. *Zingiber officinale* is used in modern Western medicine chiefly in the form of powders, extracts, distillates, infusions, tinctures, and the ethereal *Zingiber officinale* oil. It is used to prevent the symptoms of travel sickness, but also quite generally as an antiemetic. In addition, *Zingiber officinale* is used as a carminative, a spasmolytic, an antiflatulent, a digestive, an aperitive, a stomachic, an expectorant, and antitussive, an astringent, a stimulant, and a tonic.

The term "plant components" used here refers to the parts of plants which are used pharmaceutically and which thus contain the active ingredients, such parts being, for example, the leaves, fruits, and roots, including their dried forms.

The herbal preparations can be in the form of extracts, powders, distillates, infusions, tinctures, and oils.

The herbal preparation according to the invention can be in the form of capsules, film-coated tablets, solutions, sugar-coated tablets, suppositories, effervescent tablets, chewable tablets, or effervescent granulate.

The amount of the plant components used in the herbal preparation according to the invention, i.e., the amount of the preparation of *Tanacetum parthenium*, is selected so that it corresponds to 0.1-1 mg, and especially 0.2-0.6 mg, of parthenolide.

The amount of plant components or of the preparation of *Cimicifuga* used in the herbal preparation according to the invention is 20-100 mg.

The amount of plant components or of a preparation of *Vitex agnus-castus* used in the herbal preparation according to the invention is 20-100 mg, where preferably an amount of 20-40 mg is used.

The amount of plant components or of a preparation of *Zingiber officinale* used in the herbal preparation according to the invention is 0.5-6 g, where preferably an amount of 1-4 g is used.

The use of the herbal preparation according to the invention, which contains plant components and/or preparations of *Tanacetum parthenium* in combination with additional plant components selected from the group consisting of *Vitex agnus-castus* and/or *Cimicifuga racemosa* and/or *Zingiber officinale*, is intended for the treatment or prevention of migraine, especially in women in association with their periods, or of menstrual complaints or of additional gastrointestinal complaints.

Tanacetum parthenium combined with *Vitex agnus-castus*, *Tanacetum parthenium* combined with *Cimicifuga racemosa*, *Tanacetum parthenium* combined with

Zingiber officinale, and *Tanacetum parthenium* combined with *Vitex agnus-castus* and *Zingiber officinale* represent the preferred combination preparations according to the invention with respect to the use described above.

CLAIM(S)

1. Herbal pharmaceutical preparation for the treatment of migraine, characterized by the combination of *Tanacetum parthenium* with other plant components selected from the group consisting of *Vitex agnus-castus* and/or *Cimicifuga racemosa* and/or *Zingiber officinale*.

2. Herbal pharmaceutical preparation for the treatment of migraine according to Claim 1, characterized by the use of components and/or preparations of the pharmaceutically active ingredients.

3. Herbal pharmaceutical preparation for the treatment of migraine according to Claim 1 or Claim 2, characterized by preparations in the form of extracts, powders, distillates, infusions, tinctures, and oils.

4. Herbal pharmaceutical preparation for the treatment of migraine according to one of the preceding claims, characterized by the combination of *Tanacetum parthenium* with *Vitex agnus-castus*.

5. Herbal pharmaceutical preparation for the treatment of migraine according to one of the preceding claims, characterized by the combination of *Tanacetum parthenium* with *Cimicifuga racemosa*.

6. Herbal pharmaceutical preparation for the treatment of migraine according to one of the preceding claims, characterized by the combination of *Tanacetum parthenium* with *Vitex agnus-castus* and *Zingiber officinale*.

7. Herbal pharmaceutical preparation for the treatment of migraine according to one of the preceding claims, characterized by the combination of *Tanacetum parthenium* with *Zingiber officinale*.

8. Herbal pharmaceutical preparation for the treatment of migraine according to one of the preceding claims, characterized by capsules, film-coated tablets, solutions, sugar-coated tablets, suppositories, effervescent

tablets, chewable tablets, and effervescent granulate as forms of administration.

9. Herbal pharmaceutical preparation for the treatment of migraine according to one of the preceding claims, characterized by a content of *Tanacetum parthenium* in the form of the plant components and/or a preparation which contains 0.1-1 mg, and especially 0.2-0.6 mg of parthenolide.

10. Herbal pharmaceutical preparation for the treatment of migraine according to one of the preceding claims, characterized by a content of 20-100 mg of *Cimicifuga racemosa* in the form of the plant components and/or a preparation.

11. Herbal pharmaceutical preparation for the treatment of migraine according to one of the preceding claims, characterized by a content of 20-100 mg of *Vitex agnus-castus* in the form of the plant components and/or a preparation, especially 20-40 mg.

12. Herbal pharmaceutical preparation for the treatment of migraine according to one of the preceding claims, characterized by a content of 0.5-6 g of *Zingiber officinale* in the form of the plant components and/or a preparation, and especially 1-4 g.

13. Use of a composition consisting of herbal components and/or preparations of *Tanacetum parthenium* in combination with other plant components selected from the group consisting of *Vitex agnus-castus* and/or *Cimicifuga racemosa* and/or *Zingiber officinale* for the treatment or prevention of migraine, especially in women in association with their periods, or of menstrual complaints or of additional gastrointestinal complaints.

14. Use of a composition according to Claim 13, characterized by *Tanacetum parthenium* combined with *Vitex agnus-castus*, *Tanacetum parthenium*

combined with *Cimicifuga racemosa*, *Tanacetum parthenium* combined with *Zingiber officinale* , and *Tanacetum parthenium* combined with *Vitex agnus-castus* and *Zingiber officinale* as preferred combination preparations.

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY Includes Reference to PCT International Applications	Attorney's Docket No.4271-30PUS

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

PHARMACEUTICALLY ACTIVE PLANT PREPARATION FOR THE TREATMENT OF MIGRANE

the specification of which (check only one item below)

[ ] is attached hereto

[ ] was filed as United States application

Serial No. _

on

and was amended

on _ (if applicable).

[x] was filed as PCT international application

Number PCT/EP99/07045

on 22 September 1999

and was amended under PCT Article 19

on (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability of the application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed.

PRIOR FOREIGN/PCT APPLICATIONS AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. 119:

Country (if PCT, indicate "PCT")	Application Number	Date of Filing (day, month, year)	Priority Claimed Under 35 U.S.C. 119	
Germany	198 44 836.8	30 September 1998	[x] YES	[ ] NO
PCT	PCT/EP99/07045	22 September 1999	[x] YES	[ ] NO
			[ ] YES	[ ] NO
			[ ] YES	[ ] NO
			[ ] YES	[ ] NO
			[ ] YES	[ ] NO

Combined Declaration for Patent Application and Power of Attorney (Continued) (Includes Reference to PCT International Applications)	Attorney's Docket 4271-30PUS

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 U.S.C. 120:

U.S. APPLICATIONS		STATUS *(check one)*		
U.S. APPLICATION NUMBER	U.S. FILING DATE	PATENTED	PENDING	ABANDONED
PCT APPLICATIONS DESIGNATING THE U.S.				
PCT APPLICATION NO.	PCT FILING DATE	U.S. SERIAL NUMBERS ASSIGNED *(if any)*		
PCT/EP99/07045	22 September 1999		X	

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. *(List name and registration number)*

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Combined Declaration for Patent Application and Power of Attorney (Continued) (Includes Reference to PCT International Applications)				Attorney's Docket 4271-30PUS
203	FULL NAME OF INVENTOR	FAMILY NAME	FIRST GIVEN NAME	SECOND GIVEN NAME
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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201	SIGNATURE OF INVENTOR 202	SIGNATURE OF INVENTOR 203
DATE 26/03/01	DATE	DATE